PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1124WOORD01	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/09622	International filing date *(day/month/year)* 29.08.2003	Priority date *(day/month/year)* 30.08.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/58		
Applicant ALTANA PHARMA AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.03.2004	24.08.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Beranová, P Telephone No. +49 30 25901-333

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/09622

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-9 as originally filed

Claims, Numbers

1-18 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

   see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-16,18 (with respect to industrial applicability)

because:

☒ the said international application, or the said claims Nos. 1-16,18 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-14,16
	No:	Claims	1,15,17,18
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-18
Industrial applicability (IA)	Yes:	Claims	17
	No:	Claims	-

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

3.1 Claims 1 - 16 and 18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

5.1 Reference is made to the following documents:

D1: WO 02 12235 A (KATO TOMOKI ;PFIZER PHARMA (JP); SHISHIDO YUJI (JP); IKEDA TAKAFUM) 14 February 2002 (2002-02-14)

D2: US 2002/115680 A1 (PIEPER MICHAEL PAUL ET AL) 22 August 2002 (2002-08-22)

D3: WO 01 28562 A (NISHIBE YOSHIHISA ;NAGANO ATSUHIRO (JP); TEIJIN LTD (JP); TAKANASH) 26 April 2001 (2001-04-26)

D4: SCHMIDT BERNHARD M W ET AL: 'The new topical steroid ciclesonide is effective in the treatment of allergic rhinitis' JOURNAL OF CLINICAL PHARMACOLOGY, vol. 39, no. 10, October 1999 (1999-10), pages 1062-1069, XP008024248 ISSN: 0091-2700

D5: EP-A-0 903 151 (ASTA MEDICA AG) 24 March 1999 (1999-03-24)

D6: MATTILA MAURI J ET AL: 'Variations among non-sedating antihistamines: Are there real differences?' EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY, vol. 55, no. 2, April 1999 (1999-04), pages 85-93, XP002260456 ISSN: 0031-6970

5.2 **NOVELTY**

The document **D1** discloses 1,4-dihydropyridines which may be used in combination with ciclesonide and antihistamines (cetirizine, loratadine, desloratadine, fexofenadine, astemizole, azelastine, chlorpheniramine) and the use of the combination for the treatment of rhinitis (claim 18; page 25, line 31; page 23, lines 19 - 31).

D2 teaches about a composition comprising anticholinergics which may be combined

with ciclesonide and antihistaminics (claims; page 12, paragraph [0177]; page 13, paragraph [0179]).

The present application thus does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1, 15, 17 and 18 is not new in the sense of Article 33(2) PCT.

5.3 **INVENTIVE STEP**

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1 - 18 does not involve an inventive step in the sense of Article 33(3) PCT.

The documents **D3** and **D4** are regarded as being the closest prior art, and both disclose compositions comprising ciclesonide and their use for the treatment of allergic rhinitis (D3: claims 1 - 23; D4: page 1062, abstract)

The present application differs from these known D3 and D4 in that antihistamines are added to the pharmaceutical composition.

The problem to be solved by the present invention may therefore be regarded as providing for an effective treatment of allergic rhinitis.

However, the documents **D5** and **D6** both report that antihistamines are effective in the treatment of allergic rhinitis and conjunctivitis (D5: page 2, paragraphs [0002], [006] and [007]; D6: page 90, left-hand column to page 91, left-hand column).

In the absence of evidence that the combination of both agents (i.e. ciclesonide + antihistamines) is related to a new and surprising effect when compared to the use of either agent alone, it is considered that the subject-matter of claims 1, 17 and 18 lacks inventive step (Article 33(3) PCT).

The same applies to the subject-matter of the dependent claims 2 - 16 which apparently do not contain any technical features which could be regarded as inventive per se.

5.4 For the assessment of the present claims 1 - 16 and 18 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

5.5 ADDITIONAL OBSERVATIONS

Present claims 1 -14 and 16 - 18 relate to compounds defined by reference to a desirable characteristic or property, namely "antihistamine" and "osmotic pressure-controlling agent". The claims cover all compounds having this characteristic or property, whereas the application provides support and disclosure within the meaning of Article 6 PCT for only a very limited number of such compounds. Consequently, the claims lack support and the application lacks of disclosure. Independent for the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by their pharmacological profile, rendering the protection of said claims obscure. It is pointed out that a compound cannot be sufficiently characterised by its pharmacological profile or its mode of action. The use of such a functional definition is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature (i.e. the compounds) to which it refers.

It is also pointed out that a detailed description of at least one way of carrying out the invention must be given. The description must disclose any feature essential for carrying out the invention in sufficient detail to render it obvious to the skilled person how to put the invention into practice. It is a well-established and accepted principle that, for the purpose of patent protection of a medical application of a substance (or combination of substances), a pharmacological effect observed either in vitro or on animal models is required to provide evidence of a therapeutic application. In the absence of evidence that the claimed combination of ciclesonide and antihistamines has an effect on allergic rhinitis and/or allergic conjunctivitis, it is considered that claims 1 - 18 do not meet requirements of Article 5 PCT.